

REMARKS

This application is amended in a manner to place it in condition for allowance at the time of the next Official Action.

**Status of the Claims**

Claim 1 has been amended to include the features previously recited in claims 2 and 5. Accordingly, claims 2 and 5 have been cancelled.

Claims 3, 4, 6, 7 and 13 have been amended so as to be consistent with claim 1.

Claims 16-18 are amended in a manner suggested by the Examples, i.e., the compounds have shown activity in treatment of particular ailments, e.g., reduction of cholesterol and reduction in insulin levels in Example 7.

Claims 8-12 have been cancelled, without prejudice, as Applicants reserve their right to file one or more divisional applicants to the non-elected subject matter.

Claims 1, 3, 4, 6, 7 and 13-18 remain in this application.

**Claim Rejections-35 USC §112**

Claims 1-5 and 13-18 were rejected under 35 U.S.C. §112, second paragraph, for being indefinite. This rejection is respectfully traversed for the reasons below.

The position of the Official Action was that various claims included unclear language. For example, claim 1 included "possibly comprising" and "possibly substituted", claim 2 included "more particularly of fluoride" and "preferably in the para position", claims 5 and 13 included "preferentially a fluoride".

The amended claims no longer include such unclear terms, and are definite.

Therefore, withdrawal of the rejection is respectfully requested.

**Claim Rejections-35 USC §112**

Claims 1-7 and 13-18 were rejected under 35 U.S.C. §112, first paragraph, for not complying with the enablement requirement. This rejection is respectfully traversed for the reasons below.

Claim 1 is amended in a manner which is believed to be enabled by the originally filed specification.

Claim 16-18 are amended to no longer recite an intended use, but recite compounds in terms of the activity relative to the Examples of the specification. The examples show the effect of various compounds in, for example, reduction of cholesterol and reduction in insulin levels in Example 7. Thus, the specification does provide enablement

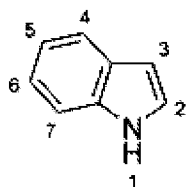
for a composition having such compounds with an activity relating to the claimed treatments.

Therefore, the present claims comply with the enablement requirement and withdrawal of the rejection is respectfully requested.

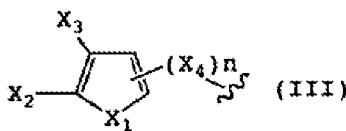
**Claim Rejections-35 USC §102**

Claims 1-5 and 13-18 were rejected under 35 U.S.C. §102(b) as being anticipated by CAI et al. U.S. 2003/0105140 A1 ("CAI"). This rejection is respectfully traversed for the reasons below.

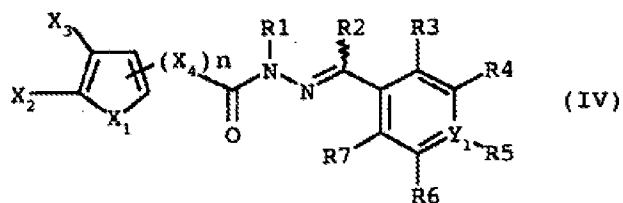
For ease of understanding, the classical IUPAC numbering concerning the substituting positions will be used, as shown on the "indole" moiety below:



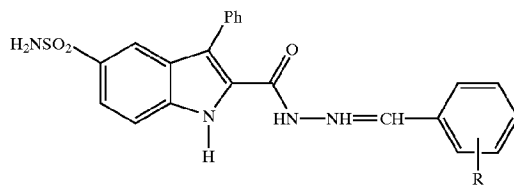
The compound according to general formula (III) of the present invention includes the following labels:



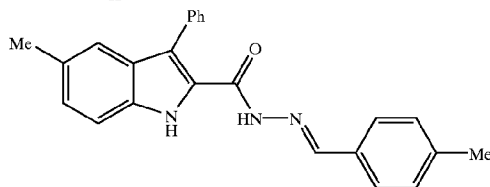
Currently amended claim 1 is now directed to compounds of general formula (IV):



The position of the Official Action CAI anticipates the claimed invention, especially in view of compounds disclosed on page 2, [0013] and page 6, [0051], which have the following chemical formulae:



and



Both of these CAI compounds are substituted on the 3-position of indole moiety by a phenyl (i.e. Ph) group.

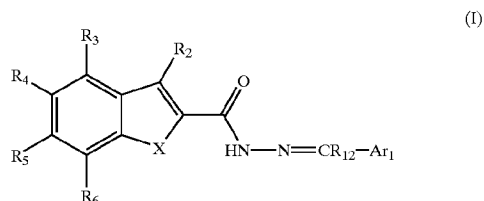
However, the compounds of general formula (IV) according to the currently amended independent claim 1 are unsubstituted on that position.

Accordingly, it is respectfully submitted that compounds disclosed on page 2, [0013] and page 6, [0051] of CAI do not fall within the scope of new proposed claim 1.

More generally, it is further submitted that none of the compounds specifically disclosed in CAI (see especially compounds disclosed in [0047] to [0128]) fall within the scope of new proposed claim 1 for one or more of the following reasons:

- (1) compounds of general formula (IV) according to the present invention are unsubstituted on the 3-position of the moiety of general formula (III) (see most of the compounds disclosed in [0047] to [0128] of CAI);
- (2) R3 to R7 substituents of the compound of general formula (IV) according to the present invention can not be a nitro group (see compounds disclosed in [0050] and [0097] (and [0108] and [0109]) of CAI); and/or
- (3) compounds of general formula (IV) according to the present invention can not contain a naphthyl moiety (see compounds disclosed in [0051] and [0052] (and [0110] and [0111]) of CAI).

Indeed, in order to even approach the claimed invention based on the general formula defined by CAI in [0033]:



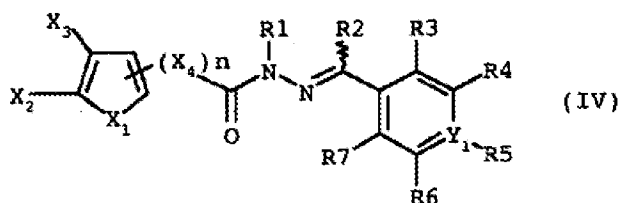
one would have had to pick and choose various substituents in a very particular combination without any guidance from CAI. Such picking and choosing is not permitted under 35 U.S.C. 102.

Therefore, currently amended independent claim 1, and the claims depending from claim 1 are not anticipated by CAI, and withdrawal of the rejection is respectfully requested.

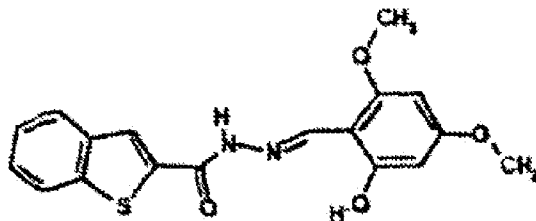
#### **Claim Rejections-35 USC §103**

Claims 1-7 and 13-18 were rejected under 35 U.S.C. §103(a) as being unpatentable over CAI. This rejection is respectfully traversed for the reasons below.

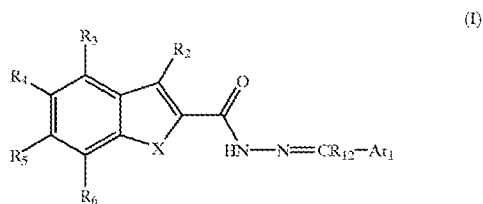
Currently amended claim 1 is now directed to compounds of general formula (IV):



Such compounds include the elected species CGP02-01, or N'-[(1E)-(2-hydroxy-4,6-dimethoxyphenyl)methylene]-1-benzothiophene-2-carbohydrazide, as recited in claim 6, which was drawn as 2,4,6 trimethoxyphenyl in Official Action, but is correctly shown below (See, e.g., page 38 of the specification):



The Official Action acknowledged that CAI fails to explicitly teach this specific compound, but the position of the Official Action was that the elected compound of the present invention is within the scope of the generic formula (I) of CAI, as shown below:



However, the claimed species and other compounds described by the general formula IV of claim 1 cannot be rendered obvious for at least two reasons:

(1) The compounds have a different function.

At the very least, the claimed compounds differ from the compounds envisioned by CAI in their therapeutical activity.

Indeed, as mentioned in [0032] and [0152] to [0154], compounds disclosed in CAI are used for treating cancer diseases.

Compounds according to the present invention are said to be useful for treating and/or preventing of diseases associated with lipid metabolism disorders, more precisely for treating and/or preventing cardiovascular diseases such as atherosclerosis, arterial restenosis, obesity, type II diabetes mellitus, cerebral ischaemia, hepatic steatosis, hypercholesterolaemia, hypertriglyceridaemia, dyslipoproteinaemia, hylomicronaemia, lipodystrophy and hyperglycaemia and atherosclerosis.

The present specification demonstrates that the elected compound CGP 02-01 was effective in, for example, blocking accumulation of intracellular lipids, e.g., in table 1 of page 29, and the reduction of cholesterol in Example 5.

Accordingly, it is respectfully submitted that compounds disclosed in CAI have a totally different



therapeutic activity compared to compounds according to the present invention.

Consequently, obtaining the claimed compounds having a different therapeutic activity than those of CAI would have been unobvious.

(2) CAI fails to provide direction to the particular elected CGP 02-01.

Indeed, CAI appears to lead one away from the elected CGP 02-01 compound. For example, in the preferred formulas of CAI, the "X" is not sulfur, but rather nitrogen. Moreover, the R2 and R4 are not hydrogen.

Thus, it would have been unobvious for one to pick and choose various substituents from non-preferred embodiments for the purpose of CAI.

Therefore, it is submitted that new proposed claim 1 (and consequently all the other proposed claims) are not obvious in view of CAI, and withdrawal of the rejection is respectfully requested.

#### **Information Disclosure Statement**

The Official Action did not consider any of the cited articles and the Japanese Abstract in the IDS file July 27, 2006. Although no reason was given, it appears that these articles were not forwarded to the USPTO from the International Search Authority. Accordingly, the Appendix

includes a courtesy copy of these documents, as noted in the IDS filed July 27, 2006, the explanation of the relevance of these documents is provided in the International Search Report.

Additionally, in reviewing these documents, it was noted that an article by Cariati et al. was cited in the International Search Report, but not in the IDS. Accordingly, this document is now provided in the accompanying IDS.

Therefore, consideration of all of these documents is respectfully requested.

### **Conclusion**

In view of the amendment to the claims and the foregoing remarks, this application is in condition for allowance at the time of the next Official Action. Allowance and passage to issue on that basis is respectfully requested.

Should there be any matters that need to be resolved in the present application, the Examiner is respectfully requested to contact the undersigned at the telephone number listed below.

The Commissioner is hereby authorized in this, concurrent, and future replies, to charge payment or credit any overpayment to our credit card which is being paid online simultaneously herewith for any additional fees required under 37 C.F.R. § 1.16 or under 37 C.F.R. § 1.17.

Respectfully submitted,

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**APPENDIX:**

The Appendix includes the following item(s):

- Patent Abstracts of Japan vol. 1999, no.09, 30 July 1999 (1999-07-30) & JP 11 106371 A (Nisshin Flour Milling Co Ltd), 20 April 1999 (1999-07-30)
- Trivedi et al. " Synthesis and antimicrobial activity of some heterocyclic compounds" Ind. J. Chem., vol. 32 B, 1993, pages 497-500, XP001181798 Compose IIe
- Georgieva et al.: "Isonicotinoylhydrazone Analogs of Isoniazid: Relationship between Superoxide Scavenging and Tuberculostatic Activities" Biochemistry (Moscow) vol. 67, no. 5, 2002, pages 588-591, XP001181795 Compose SH11.
- Patel et al.: "Studies on Antitubercular and Antibacterial Agents: preparation of 1-(4-Amino benzoyl)-2-benzalhydrazine and 1-(4-(phenylthioureido)benzoyl)-2-substituted benzalhydrazine" J. Ind. Chem. Soc., vol. 61, 1984, pages 718-720, XP001181932 Taleaul, composes 1-15.
- Shah et al.: "Studies on isoniazide derivatives. Preparation and Antimicrobial Activity of 2-Aryl-3-(pyridylcarbamoyl)-5-carboxymethyl-4-thiazolidinones" J. Ind. Chem. Soc., vol. 62, no.3, 1985, pages 255-257, XP001182001 Tableau 1, Compose 1-13.
- Dave et al.: "Studies on Thiazolidinones as potential Antitubercular Compounds" J. Indian Chem. Soc., vol. 63. no. 3, 1986, pages 320-322, XP001181800 Tableau 1, composes 1-12.
- Cowper et al.: "Studies on Aminonitriles as Drug potentials: Aminonitriles of Isoniazide" J. Inst. Chemists (India), vol. 53, no. 7, 1981, pages 195-197, XP001181937 Tableau I, composes 1, 3-10, 13.
- Grammaticakis: "No 160. - Contribution a l'etude de l'absorption dans le ultraviolet moyen et le visible des aryl- et aroyl-hydrazones. VII. - Nitrobenzoylhydrazones (o, m et p), 2e memoire" Bulletin De La Societe Chimique De France, no.3, 1970, pages 933-945, XP001181938 p. 943, composes 9, 13, 18, 19, 27 p.945 composes 31, 37, 46, 50 p.945, composes 55, 56.
- Chary et al. : "Synthesis of 2-methyl-N-(4-oxo-2-aryl-3-thiazolidinyl)-1, 8-naphthyridine-3-carboxamides" Sulfur Letters, vol. 8, no. 2, 1988, pages 79-88, XP001181799 Compose (3).
- Shilikadze et al.: Bulletin of the Academy of Sciences of the Georgian SSR, vol. 91, no. 1, 1978, pages 145-148, XP001182018 Composes sur p. 145.
- Salem: "Clinico pathological studies on some newly synthetic quinoline derivatives" J. Drug Res. Egypt, vol. 41, no. 25, 2002, pages 6597-6603, XP002284236 Composes (I) page 6598.
- Kauppi et al. L "Targeting Bacterial Virulence: Inhibitors of Type III Secretion in Yersinia" Chemistry & Biology, vol.10, no. 3, March 2003 (2003-03), pages 241-249, XP002284237 Compose 2.
- IDS with omitted reference by Cariati et al.